A Double-Blind Gastroscopic Study of a Bismuth-Peptide Complex in Gastric Ulceration

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SUMMARY

Forty courses of treatment with bicitropeptide (BCP) were administered to 30 patients with gastric ulcers, in a double-blind crossover trial. Healing was judged gastroscopically after 4 weeks, at which time 79% of ulcers had healed on BCP and 35% on placebo ($P<0,01$). There were no side-effects. Bicitropeptide is a bismuth-protein complex, active at a pH of less than 4. A protective 'protein-bismuth complex' layer is said to be formed over the ulcer.

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At present the only treatments that have been shown in controlled trials to affect the rate of healing of gastric ulcers are carbenoxolone sodium,[1] bed rest and cessation of smoking.[2] The drug carbenoxolone sodium causes the advent of side-effects in a small but significant number of patients, including salt and water retention. Symptoms may be relieved by antacids,[3] but these appear not to affect the rate of healing. In this trial, the effect of a bismuth-protein complex (bicitropeptide (BCP); Med-Nim) active at the range of acid pH (below 4,0) usually present in the stomach, has been tested in the treatment of gastric ulceration.

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METHODS

Thirty patients with benign chronic gastric ulceration seen on endoscopy were studied. Only patients with solitary ulcers on the lesser curve of the stomach in the neighbourhood of the angulus were studied. Each patient had a pretreatment barium meal, gastric acid output measured after pentagastrin,[4] in the test modified after Kay,[5] and a gastroscopy. The gastroscope employed was the side-view Olympus GF type B, which has an automatic 16-mm camera. All patients were ambulant and were given treatment with BCP or placebo in a double-blind fashion at a dose of 10 ml in 30 ml of water 4 times daily, half an hour before meals and on retiring at night, for 4 weeks. Crossover was effected if symptoms had not abated within 2 weeks. Clinical assessment was made every 2 weeks, and gastroscopic assessment was made after 4 weeks of treatment. No patient was admitted to the trial if there was a complication such as haematemesis or pyloric obstruction, or if there was coexisting duodenal ulceration. Patients were advised to avoid only those foods which appeared to produce symptoms. Smoking was not discussed, no sedatives or other drugs were given, and no change in resting habits was advised.

RESULTS

Forty courses of treatment were given to the 30 patients (Table I). Ten patients received crossover therapy (7 of

TABLE I. EFFECT OF BICITROPEPTIDE ON THE GASTROSCOPIC HEALING OF GASTRIC ULCERS AT 4 WEEKS

	Healed												Not healed
		Age of patients (yrs)					Length of history (weeks)						
		Male			Female		Male			Female			
	No. of patients	No.	M	SD	No.	M	SD	No.	M	SD	No.	M	SD	No. of patients
Bicitropeptide	**19* (79%)**	**14**	**45,7**	**10,0**	**5**	**41,4**	**11,1**	**14**	**12,0**	**13,7**	**5**	**12,7**	**13,1**	**5**
Placebo	**6 (35%)**	**4**	**35,5**	**9,0**	**2**	**46,0**	**3,0**	**4**	**11,0**	**8,1**	**2**	**9,0**	**7,0**	**10**

* $\chi^2 = 7{,}112$; $P<0{,}01$.

the 10 placebo failures were placed on BCP and subsequently healed; and 3 of the 5 BCP failures were placed on placebo and subsequently healed). As seen on gastroscopy and barium meal, at 4 weeks after onset of treatment, 19 gastric ulcers (79%) had healed on BCP. The time taken for disappearance of symptoms was 6,2 ± 3,8 days (mean ± SD). The ulcers of 5 patients did not heal completely on BCP on gastroscopy, although 3 of these had a partial response both clinically and on gastroscopy. The ulcers of 6 patients healed on placebo (35%). The mean time for disappearance of symptoms in the 6 patients whose ulcers healed on placebo was 9,5 ± 4,2 days. The ulcers of 10 patients failed to heal on placebo. A χ^2 of 7,112 was obtained in favour of BCP, which is significant at the $P<0{,}01$ level. The ages of the patients in each treatment group, and the mean length of history are shown in Table I. There were similarities in each group in age and length of history. All patients secreted acid (maximal acid output, mEq/h: males (mean ± SD) 17,9 ± 7,8; range 1,8 to 28,1; females (mean ± SD) 12,7 ± 6,2; range 0,8 to 21,3).

DISCUSSION

Bicitropeptide is a stabilised solution of soluble bismuth-proteinate complexes. The carrier proteins (peptides) appear to play an important role. These peptides allow bismuth to be liberated and exchanged with tissue protein over the range of acid pH values normally encountered in the stomach. The bismuth is then selectively transferred to the actively growing wound tissue in the ulcer. A protective 'protein-bismuth complex' layer is formed over the ulcer site, protecting it from the acid pepsin action of gastric juice, enabling healing of the ulcer to occur.[6] Trapped pepsin may be inactivated in the bismuth section of the protective layer.[6] Because BCP insulates the ulcer from the harmful acid-pepsin digestion, no concomitant therapy is indicated, such as special diets or antacids. Assays for bismuth in blood and organs of animals, and in blood and urine of humans following ingestion of BCP have failed to reveal detectable amounts of bismuth in dilutions of 3 parts per million.[6] No acute toxic or teratogenic effects have been observed in animals.[6] BCP compound has been shown to provide effective therapy in ambulant patients with gastric and duodenal ulcers.[6,7]

The present double-blind trial has demonstrated that in patients on BCP, 79% of gastric ulcers healed. In patients on placebo only 35% of ulcers healed. This is a significant result in favour of BCP (χ^2 7,112, $P<0{,}01$). No side-effects were observed in this trial, and in this respect BCP has an advantage compared with antacids, anticholinergics or carbenoxolone sodium.

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